

In the Claims:

Please amend claims 1, 3, 12, 14, 23, and 25 and add claims 34-51 as indicated below. After entry of this amendment, claims 1-20 and 23-51 will be pending in the application.

1. (Currently Amended) A method for inhibiting proliferation of cancer cells comprising:

(a) administering to the cells a first agent comprising a synthetic, modified oligonucleotide complementary to, ~~and which down-regulates expression of,~~ nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α , ~~the modified oligonucleotide and~~ having from ~~about 150~~ to ~~about 25~~ 30 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and being the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the cells a second agent comprising an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs;

wherein the administering steps may be performed simultaneously or sequentially in any order.

2. (Original) The method of claim 1, wherein the oligonucleotide is a hybrid oligonucleotide.

3. (Currently Amended) The method of claim ~~1,2~~, wherein the oligonucleotide has a nucleotide sequence consisting ~~essentially~~ of the nucleotide sequence set forth in SEQ ID NO:4.

4. (Original) The method of claim 1, wherein the second agent is an antibody that binds to EGFR.

5. (Original) The method of claim 4, wherein the antibody is a monoclonal antibody.

6. (Original) The method of claim 5, wherein the antibody is C225.

7. (Original) The method of claim 1, wherein the second agent is a taxane.

8. (Original) The method of claim 7, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel.

9. (Original) The method of claim 1, wherein the second agent is administered prior to administration of the first agent.

10. (Original) The method of claim 1, wherein the cancer cells are human cancer cells.

11. (Original) The method of claim 10, wherein the human cancer cells are selected from the group consisting of breast cancer cells, colon cancer cells, and ovarian cancer cells.

12. (Currently Amended) A pharmaceutical composition comprising:

(a) a first agent comprising a synthetic, modified oligonucleotide complementary to, ~~and which down-regulates expression of,~~ nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit R1 α , ~~the modified oligonucleotide and~~ having from about 150 to about 2530 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and being the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) a second agent comprising an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs.

13. (Previously Amended) The pharmaceutical composition of claim 12, wherein the oligonucleotide is a hybrid oligonucleotide.

14. (Currently Amended) The pharmaceutical composition of claim ~~12~~13, wherein the oligonucleotide has a nucleotide sequence consisting ~~essentially~~ of the nucleotide sequence set forth in SEQ ID NO:4.

15. (Previously Amended) The pharmaceutical composition of claim 12, wherein the second agent is an antibody that binds to EGFR.

16. (Previously Amended) The pharmaceutical composition of claim 15, wherein the antibody is a monoclonal antibody.

17. (Previously Amended) The pharmaceutical composition of claim 12, wherein the antibody is C225.

18. (Previously Amended) The pharmaceutical composition of claim 12, wherein the second agent is a taxane.

19. (Previously Amended) The pharmaceutical composition of claim 18, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel.

20. (Previously Amended) The pharmaceutical composition of claim 12, wherein the second agent is administered prior to administration of the first agent.

21. (Cancelled)

22. (Cancelled)

23. (Currently Amended) A method for treating cancer in an afflicted subject comprising:

(a) administering to the subject a first agent comprising a synthetic, modified oligonucleotide complementary to, ~~and which down-regulates expression of,~~ nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α , the modified oligonucleotide and having from ~~about 150~~ to ~~about 25~~ 30 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and being the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the subject a second agent comprising an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs,

wherein the administering steps may be performed simultaneously or sequentially in any order.

24. (Original) The method of claim 23, wherein the oligonucleotide is a hybrid oligonucleotide.

25. (Currently Amended) The method of claim 24, wherein the oligonucleotide has a nucleotide sequence consisting ~~essentially~~ of the nucleotide sequence set forth in SEQ ID NO:4.

26. (Original) The method of claim 23, wherein the second agent is an antibody that binds to EGFR.

27. (Original) The method of claim 26, wherein the antibody is a monoclonal antibody.

28. (Original) The method of claim 27, wherein the antibody is C225.

29. (Original) The method of claim 23, wherein the second agent is a taxane.

30. (Original) The method of claim 29, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel.

31. (Original) The method of claim 23, wherein the second agent is administered prior to administration of the first agent.

32. (Previously Amended) The method of claim 23, wherein the subject is a human.

33. (Previously Amended) The method of claim 32, wherein the human has a cancer selected from the group consisting of breast cancer, colon cancer, and ovarian cancer.

34. (New) The method of claim 1, wherein the oligonucleotide is an inverted hybrid oligonucleotide.

35. (New) The method of claim 34, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:6.

36. (New) The method of claim 1, wherein the oligonucleotide is an inverted chimeric oligonucleotide.

37. (New) The method of claim 36, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:1.

38. (New) The method of claim 1, wherein the oligonucleotide further comprises a 2'-O-substituted nucleotide.

39. (New) The pharmaceutical composition of claim 12, wherein the oligonucleotide is an inverted hybrid oligonucleotide.

40. (New) The pharmaceutical composition of claim 39, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:6.

41. (New) The pharmaceutical composition of claim 12, wherein the oligonucleotide is an inverted chimeric oligonucleotide.

42. (New) The pharmaceutical composition of claim 41, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:1.

43. (New) The pharmaceutical composition of claim 12, wherein the oligonucleotide further comprises a 2'-O-substituted nucleotide.

44. (New) The method of claim 23, wherein the oligonucleotide is an inverted hybrid oligonucleotide.

45. (New) The method of claim 44, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:6.

46. (New) The method of claim 23, wherein the oligonucleotide is an inverted chimeric oligonucleotide.

47. (New) The method of claim 46, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:1.

48. (New) The method of claim 23, wherein the oligonucleotide further comprises a 2'-O-substituted nucleotide.

49. (New) A method for inhibiting proliferation of cancer cells comprising:

(a) administering to the cells a first agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit $R1\alpha$, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the cells a second agent comprising an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs,

wherein the administering steps may be performed simultaneously or sequentially in any order.

50. (New) A pharmaceutical composition comprising:

(a) a first agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α , and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) a second agent comprising an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs.

51. (New) A method for treating cancer in an afflicted subject comprising:

(a) administering to the subject a first agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α , and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the subject a second agent comprising an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs,

wherein the administering steps may be performed simultaneously or sequentially in any order.